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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Environmental Fate and Effects Division Risk Assessment for the Section 3 New Use Registration of Difenoconazole

TO: Janet Whitehurst, Chemical Review Manager
Tony Kish, Review Manager
Registration Division (7505P)

FROM: Holly Galavotti, Environmental Protection Specialist Holly Galavotti
Iwona Maher, Chemist IM for Margaret Rice
Tom Bailey, Branch Chief Tom A. Bailey
Environmental Risk Branch I
Environmental Fate and Effects Division (7507P)

Please find the attached Environmental Fate and Effects Division's (EFED) environmental risk assessment for the proposed new use registration of difenoconazole. Difenoconazole is a broad spectrum, preventive fungicide recommended for the control of many important plant diseases. It was first registered in Aug 4, 1994. The existing difenoconazole uses include wheat, triticale, and canola seed treatment. The proposed-label evaluated in this risk assessment is Inspire® (100-XXXX) for use on fruiting vegetables, pome fruit, vegetables subgroup (tuberous and corm), sugar beets, and ornamentals. The maximum proposed single application rate is 0.13 lb a.i./A with annual maximum of 0.56 lb a.i./A to ornamentals, and the single maximum application rate to food uses is 0.11 lb a.i./A, or less, with annual maximum up to 0.44 lb a.i./A.

Environmental fate and transport data indicate that difenoconazole is persistent (laboratory and field half-lives ($t_{1/2}$) ranged from 85 days to over 1 year), and slightly mobile in the soil environment. Difenoconazole is persistent in the soil environment with biodegradation, hydrolysis, and soil photolysis occurring slowly. In aquatic environment,

difenoconazole's main route of dissipation is partitioning into the bottom sediment as shown in an aerobic aquatic metabolism study, in which the distribution ratio of sediment and water phases was 8:1 at 1 day post treatment and 40:1 at 30 days post treatment. Difenonconazole undergoes potentially relatively fast to slow aqueous photolysis in clear water conditions.

Volatilization from soil and water surfaces is not expected to be an important process since difenoconazole has a relatively low vapor pressure (3.32e-5 mm Hg) and solubility in water of 15 mg/L. The overall stability of the compound suggests that difenoconazole will tend to accumulate in the soil with successive application year to year. Difenoconazole has potential to reach surface water via run-off, erosion, and spray drift, and is less likely to reach ground water.

A screening-level (Level I) risk assessment, based on proposed uses, suggests that levels of difenoconazole in the environment, when compared with minimum toxicity values, are likely to result in acute and chronic risk to certain aquatic organisms and chronic risk to birds and mammals. Specifically, Risk Quotient (RQ) values for those taxonomic groups exceed Levels of Concern (LOCs) established by the Agency for the screening-level risk assessment. Based on the potential for direct effects to these taxa, there may be potential indirect effects to species of concern that depend on these taxa as a source of food, habitat, pollination, etc. Specific risks to non-target organisms are summarized as follows:

Aquatic Organisms

Freshwater fish and aquatic invertebrates; estuarine/marine fish and mollusks; and aquatic plants are not at risk acutely from exposure to difenoconazole at the proposed application rates. LOCs were exceeded for the following proposed uses:

- Chronic LOCs are exceeded for freshwater and estuarine/marine fish only for the Maine potato PRZM EXAMS scenario (representing tuberous and corm vegetables; RQ = 1.14 – 1.25).
- Chronic LOCs are exceeded for freshwater invertebrates for the Maine potato, North Carolina sweet potato (representing tuberous and corm vegetables) and the New Jersey ornamental PRZM EXAMS scenario (RQ = 1.08 – 2.04).
- Acute Endangered LOCs are exceeded for estuarine/marine crustaceans (mysid shrimp) for the Maine potato, North Carolina sweet potato, and the New Jersey ornamental PRZM EXAMS scenarios (0.05 – 0.083).
- Chronic LOCs are also exceeded for estuarine/marine crustaceans for all of the uses with RQs almost two orders of magnitude greater than the LOC of 1.0 (RQ > 11.22 – 99.13).

Terrestrial Organisms

Avian and mammalian acute RQs are less than LOCs for all of the proposed crops. Avian chronic RQs exceed LOCs with values ranging from 1.36 to 4.68 for all

food groups, except fruits, pods, seeds, and large insects. Mammalian dose-based chronic RQs exceed LOCs for all of the proposed uses with values ranging from 1.02 to 35.60 for mammals up to 1000 grams consuming all modeled food groups except seeds. Mammalian dietary-based chronic RQs also exceed LOCs for all of the proposed uses with values ranging from 1.19 to 4.10 for mammals consuming all modeled food groups except fruits, pods, seeds, and large insects.

Risk quotients were not calculated for terrestrial plants because the results of the toxicity study were qualitative. The phytotoxicity test included observations of visible effects on seedling emergence and vegetative vigor. It was determined that the potential for difenoconazole to have adverse effects on terrestrial plants is low.

EFED currently does not quantify risks to terrestrial non-target insects, however, difenoconazole was classified as practically non-toxic based on the acute contact honey bee study (LD_{50}>100 µg/bee); therefore, the potential for this fungicide to have adverse effects on pollinators and other beneficial insects is low.

Listed Species

The LOCATES database (version 2.10) was used to identify federally-listed endangered or threatened species in the United States where the proposed crops are grown. Growing areas for these crops encompasses most of the United States and therefore, there are several hundred species which are found in counties where the proposed crops are grown. By tabulation of the number of unique listed species that occur in the same county of difenoconazole use, by crop and by state, the proposed uses with the highest numbers of potentially affected listed species are ornamentals (997 species), followed by fruiting vegetables (980 species), tuberous and corm vegetables (927 species), pome fruit (884 species) and sugarbeets (123 species). Currently, none of the listed taxa can be discounted since for many, direct effects are expected and, in addition, indirect effects may be important for some species in all taxa given the risks of difenoconazole. A more refined assessment should involve clear delineation of the action area associated with uses of difenoconazole and best available information on the temporal and spatial co-location of listed species with respect to the action area. This analysis has not been conducted for this assessment.

Key Uncertainties and Data Gaps

- Difenoconazole may break down to form triazolyl acetic acid and further to triazole methanol and triazole. 1,2,4-Triazole and its conjugates (triazole alanine and triazole acetic acid) are common metabolites to the class of compounds known as the triazole-derivative fungicides (T-D fungicides, conazoles). A separate cumulative risk assessment was conducted on 1,2,4-trizole degradates. The Office of Pesticide Program's Health Effects Division (HED) has conducted aggregate human health risk assessments for 1,2,4-triazole and triazole conjugates which was completed on Feb 7, 2006 (D320683). The Tier II drinking water assessment for 1,2,4-triazole was completed in Feb 28, 2006 (D320682). The potential adverse effect of triazole on the

ecological environment for the proposed uses was not addressed in this risk assessment.

- Before difenoconazole breaks down to triazole, it forms CGA205375, (1-[2-Chloro-4-(4-chlorophenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ethanol). CGA205375 has potential to be slightly more mobile in the soil than difenoconazole, based on the registrant-submitted adsorption/desorption study. The potential adverse effect of this degradate on the ecological environment was not addressed in this risk assessment. If this degradate is shown to have potential ecological or human health concern, additional fate and transport studies may be requested at later time.

- No data were available to assess the chronic toxicity of difenoconazole to estuarine/marine fish. The LC_{50}s for estuarine/marine fish were comparable to the LC_{50}s for freshwater fish, suggesting similar acute sensitivity to difenoconazole. In the absence of data, the acute to chronic ratio (ACR) from the freshwater fish data was used to estimate a NOAEC for estuarine/marine fish. The most conservative acute value of 819 µg ai/L was used for estuarine/marine fish. The most sensitive LC50 value for freshwater fish (810 µg ai/L, rainbow trout) and chronic NOAEC value (8.7 µg ai/L, fathead minnow) were used to estimate a fish ACR. An estimated NOAEC value of 8.8 µg ai/L was derived for estuarine/marine fish. Uncertainties with this calculation include species sensitivity and extrapolation error, given that quantified sensitivity factors do not currently exist. The ACR relied on extrapolating from freshwater to estuarine/marine environments and between two freshwater fish species, the rainbow trout and the fathead minnow, which may have different sensitivities to this chemical.

- Chronic estuarine/marine crustacean toxicity was based on a mysid shrimp life cycle toxicity test which resulted in a non-definitive NOAEC < 0.115 µg ai/L for reproductive effects (number offspring/female/reproduction day). There were significant adverse effects on reproductive success at all treatment levels compared to the negative control (42-68%). There is uncertainty associated with the calculated non-definitive RQ values for chronic effects to mysid shrimp which range from >11.22 to > 99.13 for all the proposed uses.

- A qualitative phytotoxicity test (including observations of visible effects on seedling emergence and vegetative vigor) was carried out on terrestrial plant species. No phytotoxic effects were observed in any species at the five treatments tested following pre- or post-emergence application (NOAEC > 0.44 lb a.i./A). At the proposed application rates, adverse affects to non-target terrestrial plants are not expected based on the visually phytotoxicity; however, there are uncertainities associated with these conclusions because definitive RQs cannot be calculated.

- There is uncertainty associated with risk to sediment dwelling organisms. Because difenoconazole is persistent and partitions to the sediment, risk to sediment dwelling organisms should be evaluated, however, a toxicity study was not provided. PRZM EXAMS estimated pore water concentrations indicated that the concentrations of

difenoconazole in the sediment are similar to that in the water column. A sediment toxicity test study determining the toxicity of difenoconazole residues to benthic organisms would reduce this uncertainty.